No. 2024-2211

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

NOVARTIS PHARMACEUTICALS CORPORATION, *Plaintiff-Appellant*

v.

MSN PHARMACEUTICALS INC., MSN LABORATORIES PRIVATE LIMITED, MSN LIFE SCIENCES PRIVATE LIMITED, GERBERA THERAPEUTICS, INC., *Defendants-Appellees*

Appeals from the United States District Court for the District of Delaware, Nos. 20-2930-RGA and 22-1395-RGA, Judge Richard G. Andrews.

NOVARTIS PHARMACEUTICALS CORPORATION'S NON-CONFIDENTIAL EMERGENCY MOTION FOR INJUNCTION PENDING APPEAL AND TO EXPEDITE

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AUGUST 13, 2024

CERTIFICATE OF INTEREST

Counsel for Novartis Pharmaceuticals Corporation certify under Federal Circuit Rule 47.4 that the following information is accurate and complete to the best of their knowledge:

1. **Represented Entities.** Provide the full names of all entities represented by undersigned counsel in this case.

Novartis Pharmaceuticals Corporation.

2. **Real Parties in Interest.** Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities.

None.

3. **Parent Corporations and Stockholders.** Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities.

Novartis AG.

4. **Legal Representatives.** List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court.

McCARTER & ENGLISH, LLP: Daniel M. Silver, Alexandra M. Joyce.

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VENABLE LLP: Christina Schwarz, Nicholas N. Kallas, Gregory J. Manas, Laura K. Fishwick, Melinda R. Roberts, Shannon K. Clark, Susanne L. Flanders, Whitney M. Howard, Maliheh Zare

5. **Related Cases.** Other than the originating case(s) for this case, are there related or prior cases that meet the criteria under Fed. Cir. R. 47.5(a)?

No.

6. **Organizational Victims and Bankruptcy Cases.** Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees).

Not applicable.

Dated: August 13, 2024

/s/ Deanne E. Maynard
Deanne E. Maynard

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CONFIDENTIAL MATERIAL OMITTED

In the non-confidential version of this brief, pages 2, 13, 22-23, and 25-26 omit material describing Novartis's and MSN's confidential financial information and MSN's manufacturing information.

TABLE OF AUTHORITIES

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TABLE OF ABBREVIATIONS

ANDA	Abbreviated new drug application
API	Active pharmaceutical ingredient
FDA	United States Food and Drug Administration
TVS	Trisodium valsartan sacubitril complex

FEDERAL CIRCUIT RULE 8 STATEMENT

Novartis Pharmaceuticals Corporation seeks an immediate temporary injunction pending this motion's resolution and an emergency injunction pending appeal enjoining MSN from launching at risk a competing generic equivalent of Novartis's patented drug ENTRESTO®.[1] This suit is one of several necessitated by the efforts of MSN and other generic drugmakers to seek FDA approval for generic products before the expiration of Novartis's patents. On July 24, 2024, the FDA approved MSN's ANDA to market a generic equivalent. The parties had previously agreed to allow time for court proceedings on injunctive relief before any at-risk launch, but the district court declined to extend that agreement on August 1, 2024. Add112-114; Add213-82. The district court instead invited the parties to brief any request for emergency injunctive relief with the expectation that MSN is planning an imminent launch. Oral Order, *In re Entresto (Sacubitril/Valsartan) Pat. Litig.*, No. 1:20-md-02930 (D. Del. Aug.1, 2024), ECF1420. On August 2, Novartis moved in district court for a preliminary injunction in this proceeding involving U.S. Patent No. 11,096,918 or in the alternative "a stay of any at-risk launch" long enough for Novartis to seek relief in this Court. Add283-309. Novartis also sought an injunction pending resolution of its fully briefed appeals in a separate action

[1] "MSN" refers collectively to MSN Pharmaceuticals Inc., MSN Laboratories Private Limited, and MSN Life Sciences Private Ltd.

involving U.S. Patent No. 8,101,659. Mot. Rule 62(d) Inj. Pending Appeal, *In re Entresto (Sacubitril/Valsartan) Patent Litig.*, ECF1432. After a hearing, the district court ordered the parties "to maintain the status quo" until it ruled. Order, *In re Entresto*, ECF1455. On August 12, 2024, at approximately 2PM ET, the district court denied Novartis's request for a preliminary injunction on the '918 patent but granted a limited 72-hour "stay to allow Novartis to seek injunctive relief from the Federal Circuit," again ordering the parties "to maintain the status quo." Add10 (internal citation omitted). The district court stated that Novartis failed to show it was likely to succeed in proving infringement. Add4-6. The district court also stated that Novartis failed to demonstrate irreparable harm because it believed Novartis's harms could be remedied with monetary damages that MSN would have the ability to pay. Add6-9. And it believed the equities weighed against an injunction. Add9-10.

Novartis seeks an immediate injunction, pending this Court's resolution of this motion for an injunction pending appeal, and then an injunction pending resolution of Novartis's appeal. Separately, Novartis is filing a motion in this Court seeking an injunction pending appeal in Appeal Nos. 2023-2218, 2023-2219, 2023-2220, and 2023-2221. Novartis notified MSN of this motion. MSN opposes and agreed to respond within 3 days (on Friday, August 16, 2024) with Novartis to reply within 3 days (on Monday, August 19, 2024).

INTRODUCTION

Novartis scientists created a lifesaving heart-failure treatment: a new pharmaceutical combination of two drugs, valsartan and sacubitril. Sold as ENTRESTO®, the combination therapy has become the preferred first-line treatment for heart failure in adults with reduced ejection fraction—and Novartis's top-selling drug.

MSN intends to launch at-risk its generic competitor, which infringes patents Novartis holds related to its groundbreaking valsartan-sacubitril treatment. Here, the '918 patent claims a novel form of the valsartan-sacubitril combination: a compound comprising anionic valsartan, anionic sacubitril, and sodium cations non-covalently bound in a 1:1:3 molar ratio ("TVS"). The '918 patent specifically claims the amorphous solid form of this compound.

This Court should temporarily enjoin MSN's launch pending this appeal on Novartis's preliminary-injunction motion. Novartis is likely to succeed on appeal because the district court made multiple errors.

First, the district court incorrectly read a limitation into the term "an amorphous solid form of a compound," believing it required the amorphous form of TVS to "predominate" over an unrecited form, crystalline TVS. But neither the claim language, the specification, nor the prosecution history supports giving the claim anything other than its plain meaning: amorphous TVS means amorphous

TVS. And because expert testing reveals that MSN's products contain amorphous TVS, they infringe.

MSN's generic infringes under the district court's construction too. That construction requires that when both amorphous TVS and crystalline TVS are present, amorphous TVS must predominate over crystalline TVS. Testing reveals that MSN's products contain no crystalline TVS, so the amorphous form of TVS necessarily predominates. The district court erred in finding Novartis was not likely to so prove.

Second, introducing a generic ENTRESTO® competitor will inflict massive financial damage to Novartis. That damage will be irreparable, including because it will permanently erode ENTRESTO®'s price; cannot be accurately calculated; and MSN financial information. The district court concluded otherwise by adopting MSN's unsupported assertions and overlooking the many decisions from this Court recognizing that similar facts suffice to show irreparable harm.

Finally, the equities further favor an injunction pending appeal. Again, the harm to Novartis from generic launch will be irreparable. The public interest will also suffer: the public has a strong interest in honoring the bargain of disclosure for a limited patent term, and a premature launch will imperil Novartis's ability to maintain programs benefiting physicians and patients.

The Court should immediately enjoin MSN's launch pending this motion's resolution, and then enjoin MSN's launch pending appeal, with expedited briefing and argument as soon as practicable.

BACKGROUND

A. The '918 Patent Claims an Amorphous Solid Form of Trisodium Valsartan-Sacubitril Complex

Novartis scientists developed multiple inventions on the path to ENTRESTO®, which has become the preferred first-line therapy for heart failure in adults with reduced ejection fraction. Add916(¶26). As relevant here, the '918 patent claims a "dual-acting compound" or "complex" of two active ingredients: valsartan and sacubitril. The "complex" is a supramolecular structure in which anionic valsartan, anionic sacubitril, and sodium cations are non-covalently bound in a 1:1:3 molar ratio. Add92(col.6:55-61). That structure is "beneficial over" "simply physically mixing two active agents," thus improving "use as a first line therapy, ease of formulation, and ease of manufacture." Add98(col.17:46-51); Add103(col.28:27-32).

Claim 1 of the '918 patent recites:

> 1. An amorphous solid form of a compound comprising anionic (S)-N-valeryl-N-{[2'-(1H-tetrazole-5-yl)-biphenyl-4-yl]-methyl}-valine, anionic (2R,4S)-5-biphenyl-4-yl-4-(3-carboxy-propionylamino)-2-methyl-pentanoic acid ethyl ester, and sodium cations in a 1:1:3 molar ratio.

Add105(col.32:42-46). The recited chemical names refer to valsartan and sacubitril. Add792-793(¶11). Anionic valsartan and anionic sacubitril have charges balanced by sodium cations when combined in a 1:1:3 molar ratio. Add792-793(¶11). The resulting non-covalent bonds yield a complex referred to as Trisodium Valsartan Sacubitril, or "TVS." Add792-792(¶11); Add742(¶12). The claims cover TVS in an "amorphous" form (meaning a form lacking long-range three-dimensional order) as opposed to a crystalline form (which has an ordered, repeating, three-dimensional pattern).

The specification explains that the claimed compound "is characterized by very distinct spectral peaks and shifts that are not observed in the physical mixture." Add98(col.17:46-58). A skilled artisan would understand that this refers to spectroscopic analytical techniques, including Raman spectroscopy, disclosed in the specification. Add793(¶13). Raman spectroscopy uses scattering from a laser to identify substances by "comparing the experimental Raman spectra obtained from the sample to the reference Raman spectra of known compounds." Add793(¶13); Add799-800(¶¶36-37). It can "detect the presence of non-covalent bonds between valsartan and sacubitril," which "are not present in a physical mixture." Add742(¶13).

Example 1 of the '918 patent describes a process for making a "glassy solid" using starting materials including sacubitril free acid and valsartan free acid.

Add103(col.28:37-54). A person of skill would have understood that the "glassy solid" disclosed in Example 1 is amorphous TVS. Add882-884(¶¶114-116); Add744-756(¶¶19, 22-23, 25-42); Add344(897:11-19).

In this MDL proceeding, the district court "stated on the record" after trial that it was "going to find for Novartis" on other generic manufacturers' invalidity challenges to the '918 patent. Add343-348(896:24-901:7). It then read from the bench a decision explaining the reasons why it would uphold the patent's validity. Add343-348(896:24-901:7) (subsequently settled). The patent expires on November 8, 2026. Add83.

B. Novartis Sued MSN for Infringement of the '918 Patent

Novartis sued MSN for infringement of the '918 patent after MSN sought approval to market generic ENTRESTO®. Add38. Expert discovery is ongoing, with trial scheduled in December 2024. Add130-131.

1. Claim construction

The sole disputed phrase was "[a]n amorphous solid form of a compound." Add141. The district court construed that phrase to mean "a solid form of a compound in which the amorphous form of the compound predominates." Add16. In doing so, it rejected Novartis's argument that the claim language should be given its plain meaning. Add16; Add141-150; Add165-175. The court also rejected MSN's position that "[a]n amorphous solid form of a compound" really meant "*a*

substantially pure amorphous solid form of a compound." Add16; Add19 (emphasis added). Instead, the district court construed the disputed term to mean that "[a]n amorphous solid form is mutually exclusive from a crystalline solid form, but not necessarily mutually exclusive from a partially crystalline solid form." Add16.

2. Preliminary-injunction proceedings

On July 24, 2024, the FDA approved MSN's ANDA. Add216. Novartis sought a preliminary injunction; MSN opposed, asserting no validity challenge; and the district court heard argument. Add1, 4; Add285-309; Add1329-1423; Add1301-1328.

On August 13, 2024, the district court denied Novartis's preliminary-injunction request but granted a limited 72-hour "stay to allow Novartis to seek injunctive relief from the Federal Circuit." Add10 (citation omitted). In so ruling, the district court applied its claim construction and concluded Novartis was unlikely to prove that the amorphous TVS in MSN's products predominates over the crystalline TVS. Add4-6. It also concluded the balance of the harms weighed against a longer injunction. Add9-10.

In addition to seeking relief here, Novartis has challenged MSN's approval under the Federal Food, Drug, and Cosmetic Act. *Novartis Pharms. v. Beccera*, No. 1:24-cv-2234 (D.D.C.).

ARGUMENT

All factors favor enjoining MSN from launching: Novartis has a strong likelihood of prevailing on appeal because it is likely to show infringement and will suffer immense and irreparable harm absent injunctive relief; and the equities and public interest warrant an injunction. *Standard Havens Prods. v. Gencor Indus.*, 897 F.2d 511, 512 (Fed. Cir. 1990).

I. NOVARTIS WILL LIKELY SUCCEED ON APPEAL

A. Novartis Will Likely Show Infringement

The district court applied the wrong claim construction, and Novartis likely will prove infringement under the correct construction. Novartis is likely to prove infringement under the district court's construction too, and the court erred in concluding otherwise.

1. The district court erroneously read limitations into the claims, and Novartis will likely prove infringement under the correct construction

Where a district court bases a preliminary-injunction ruling on an earlier claim construction, this Court has jurisdiction to review that construction in a preliminary-injunction appeal. *Microchip Tech. v. Scenix Semiconductor*, No. 99-1300, 2000 WL 945308, at *2-3 (Fed. Cir. June 16, 2000). This Court reviews claim constructions de novo where, as here, they turn on interpreting intrinsic evidence. *Id.*

a. The district court erred in construing "an amorphous solid form of a compound" as requiring comparison to an unclaimed form

Claim 1 of the '918 patent is drawn to "an amorphous solid form of [TVS]" and nothing more. Add105(col.32:42-46). The court's construction, though, requires "a solid form of a compound in which the amorphous form of the compound predominates"—meaning the amorphous TVS form must "predominate" over another form "of the compound," that is, over any crystalline TVS present. Add16. This was error.

The plain claim language does not require comparing the claimed amorphous TVS to the unclaimed crystalline TVS, let alone require that amorphous TVS "predominate" over crystalline TVS. Add105(col.32:42-49). Nor does the specification or prosecution history. Add90-108; Add187-199. Indeed, none of the intrinsic evidence suggests that comparing amorphous and crystalline TVS is necessary for a skilled artisan to determine what subject matter falls within claim 1's scope. Add90-108; Add187-199. Claim 1 is explicit in what it covers: "[a]n amorphous solid form of a compound comprising anionic [valsartan], anionic [sacubitril] and sodium cations in a 1:1:3 molar ratio." Add105(col.32:42-49). No further construction is required.

As the district court itself acknowledged, the amorphous and crystalline forms of TVS are distinct and "mutually exclusive." Add18-19. In view of the undisputed

categorical distinction between amorphous TVS and crystalline TVS, any comparison between them to determine which "predominates" is superfluous to understanding claim 1. Amorphous TVS is amorphous TVS. Its presence in any environment (including in MSN's products) by itself infringes claim 1—without regard to whether the unclaimed crystalline form of TVS also is present alongside amorphous TVS, and in what amounts.

Nothing Novartis said during prosecution disclaimed the claims' plain meaning. Although the district court pointed to a non-obviousness declaration submitted during prosecution of the '918 patent (Add17-18; Add21-22), that declaration, by Dr. Michael Cima, neither supports the district court's construction nor invites any comparison of the claimed amorphous TVS to unclaimed crystalline TVS. It does precisely the opposite. Dr. Cima's declaration notes the ways in which amorphous and crystalline forms differ generally, and asserts that, just because a crystalline form of a particular compound can be made, an amorphous form of that compound would not be easier to make and would not be obvious from the crystalline form. Add201-212. Ultimately, Dr. Cima's declaration stands for the proposition that amorphous TVS is its own unique invention from other TVS forms, like crystalline. In any event, nothing in that declaration dictates a claim construction: a "description of characteristics does not redefine a compound with

an established and unambiguous structural definition." *SmithKline Beecham v. Apotex*, 403 F.3d 1331, 1339 (Fed. Cir. 2005).

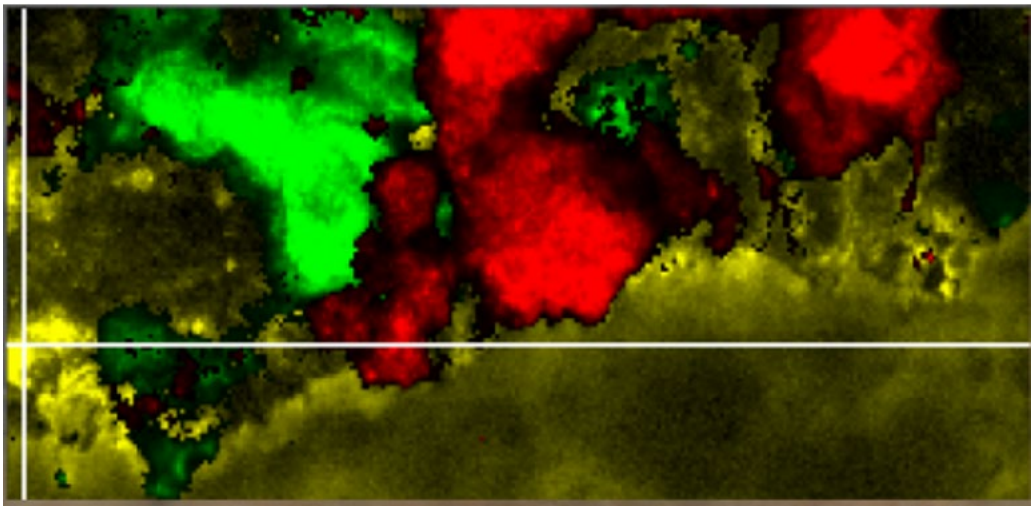
Last, because the intrinsic evidence for the '918 patent itself provides no support for the district court's construction, the court improperly looked to a purity limitation in different claims from a related set of patents—Nos. 8,877,938 and 9,388,134. Add16-17. The '938 and '134 patents disclose and claim a different invention: crystalline trisodium sacubitril-valsartan hemipentahydrate ("crystalline TSVH"). During claim construction for those patents, the district court imposed a "substantially pure" limitation on claims drawn to crystalline TSVH. *In re Entresto (Sacubitril/Valsartan) Pat. Litig.*, No. 20-mc-2930-LPS, 2021 WL 2856683, at *4-5. (D. Del. July 8, 2021); Add37. Because the "substantially pure" limitation in the '938 and '134 patents required considering unclaimed substances that might be present alongside crystalline TSVH (*i.e.*, potential impurities of crystalline TSVH), the district court reasoned that the presence of unclaimed substances also needed to be considered for claim 1 of the '918 patent. That was error.

During prosecution of the '938 and '134 patents, Novartis and the Examiner agreed that claims directed to crystalline TSVH should include a "substantially pure" limitation. Add189; Add197-198. But there was no similar colloquy or agreement between Novartis and the Examiner during the '918 patent prosecution. Nor was there any other indication in the intrinsic evidence for the '918 patent that its

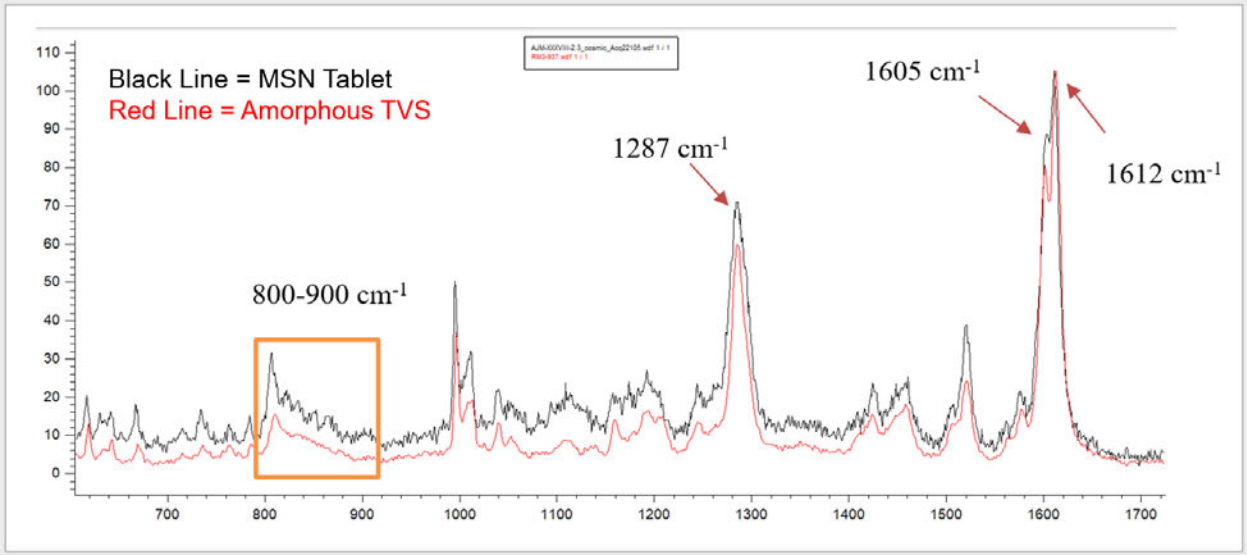
claims—drawn to amorphous TVS, a different invention—should include a "substantially pure" limitation. Because the crystalline TSVH claims of the '938 and '134 patents differ materially from the amorphous TVS claims of the '918 patent, and arise from a different prosecution history, the district court erred in relying upon the "substantially pure" limitation of those different patents to justify limiting the '918 patent's claims. *See Ventana Med. Sys., Inc. v. Biogenex Lab'ys, Inc.*, 473 F.3d 1173, 1182 (Fed. Cir. 2006) ("[T]he doctrine of prosecution disclaimer generally does not apply when the claim term in the descendant patent uses different language.").

b. Under the proper construction, Novartis is likely to prove infringement

Under the correct construction, MSN's products will infringe because they contain amorphous TVS, as demonstrated by testing conducted by Novartis's expert, Dr. Adam Matzger. Add810-823(¶¶57-73). Dr. Matzger collected thousands of experimental Raman spectra from samples of MSN's products. Add799-800(¶¶36-37); Add465-546. Dr. Matzger then compared those experimental Raman spectra to reference Raman spectra to map the substances found in the samples. Add812-822(¶¶60-68). This comparison revealed regions of separate crystalline valsartan disodium (green), separate crystalline sacubitril sodium (red), and amorphous TVS (bright yellow) within the ANDA products:



Add814(¶61). Experimental Raman spectra from the regions shown in bright yellow show amorphous TVS in MSN's products. The spectrum below illustrates the close match between Dr. Matzger's experimental Raman spectra from these regions (black) and the reference spectrum for amorphous TVS (red).



Add1308; Add815-816(¶62).

The amorphous TVS reference spectrum in red was provided by Dr. Park, another of Novartis's experts, who prepared and characterized amorphous TVS

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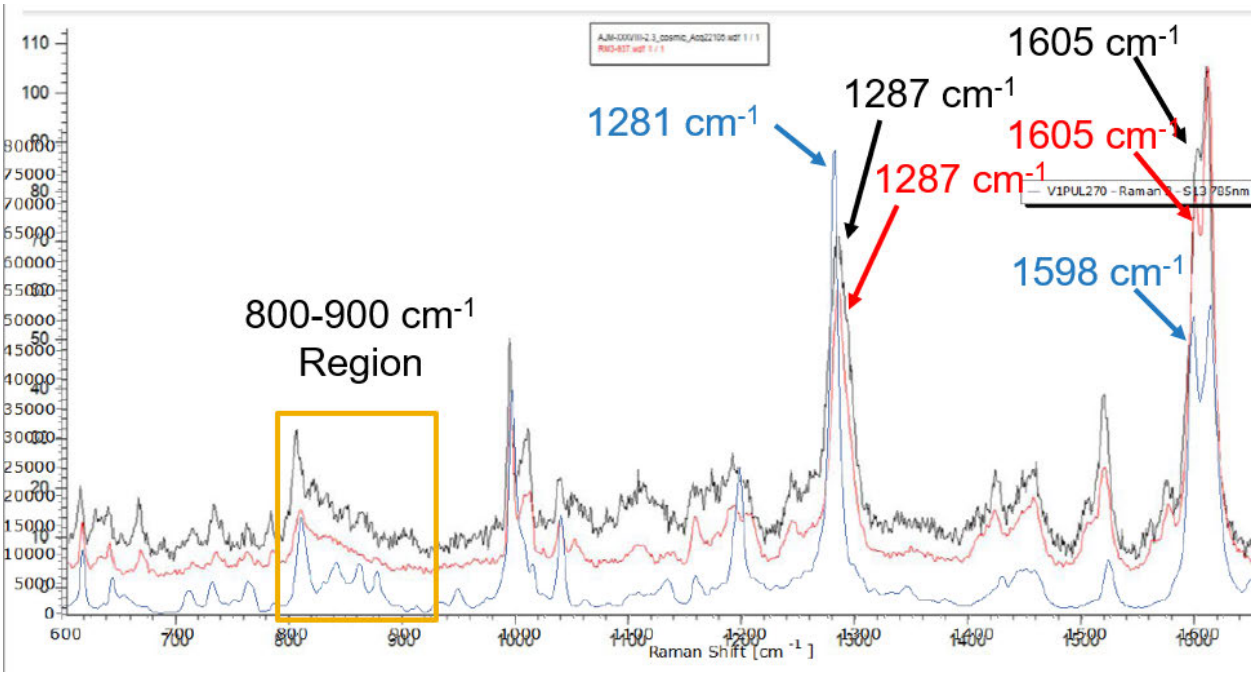
using techniques described in the patent. Add799-800(¶37); Add745-751(¶¶22-23, 29-33); *see* Add430-431; Add444; Add746-759(¶¶25-28, 34-38, 47); Add344-345(897:11-898:2). Dr. Matzger's experimental spectra display the distinctive spectral properties of amorphous TVS shown in the reference spectrum: peaks at about 1287 cm^{-1}, 1605 cm^{-1} and 1612 cm^{-1}, and, in the 800–900 cm^{-1} range, an upward slope over a small frequency range peaking around 810 cm^{-1} followed by a downward-sloping portion lacking clearly defined peaks. Add814-819(¶¶61-63); *see* Add828-830(¶¶90-96) (explaining why this combination of features is helpful to distinguish amorphous TVS). No other material in MSN's products besides amorphous TVS displays this combination of spectral features. Add812-830(¶¶60-65, 89-96). These results therefore show that MSN's products contain infringing amorphous TVS.

Dr. Matzger's experimental spectrum matches his reference for amorphous TVS better than it matches any other reference spectrum in this case. Add828-830(¶¶90-96). And Dr. Matzger also explained how amorphous TVS is introduced into MSN's product: [redacted] MSN manufacturing information [redacted] Add822-823(¶72); Add697; Add703; Add651; Add655; Add550.

The district court had no basis to disagree. Citing MSN's argument that the Raman peaks on which Dr. Matzger relies to identify amorphous TVS "more closely match the peaks in MSN's Form-S reference spectra than those in the amorphous reference spectra," the district court thought MSN's expert "undermines Dr. Matzger's conclusions." Add5. But the supposed "match" with "Form S"—MSN's isolated active pharmaceutical ingredient (API)—is illusory. The figure below compares Dr. Matzger's experimental testing spectrum (black) with Dr. Park's amorphous TVS reference spectrum (red) and MSN's reference spectrum for "Form S" (blue).



Add1326; Add1295. The overlaid spectra show that the experimental spectrum (black) better matches the amorphous reference (red) than it does MSN's "Form S" reference spectrum (blue). For example, the experimental spectrum (black) and

amorphous reference (red) both include the downward slope without distinct peaks from 810-900 cm^{-1} and matching peaks at 1287 and 1605 cm^{-1}. *See* Add815-816(¶62), Add830-831(¶¶95-96). The strong match between the experimental spectrum Dr. Matzger collected and the amorphous reference spectrum proves there is amorphous TVS in MSN's products.

In short, with Dr. Matzger's testing, Novartis's showing of infringement under the correct claim construction will be straightforward: regardless of the make-up of the rest of MSN's generic products, they contain small regions of amorphous TVS. Those regions are enough to infringe. *See SmithKline*, 403 F.3d at 1341 (affirming that even "trace amount" of claimed compound in accused ANDA product infringes). The district court clearly erred in finding Novartis unlikely to meet its burden to so prove.

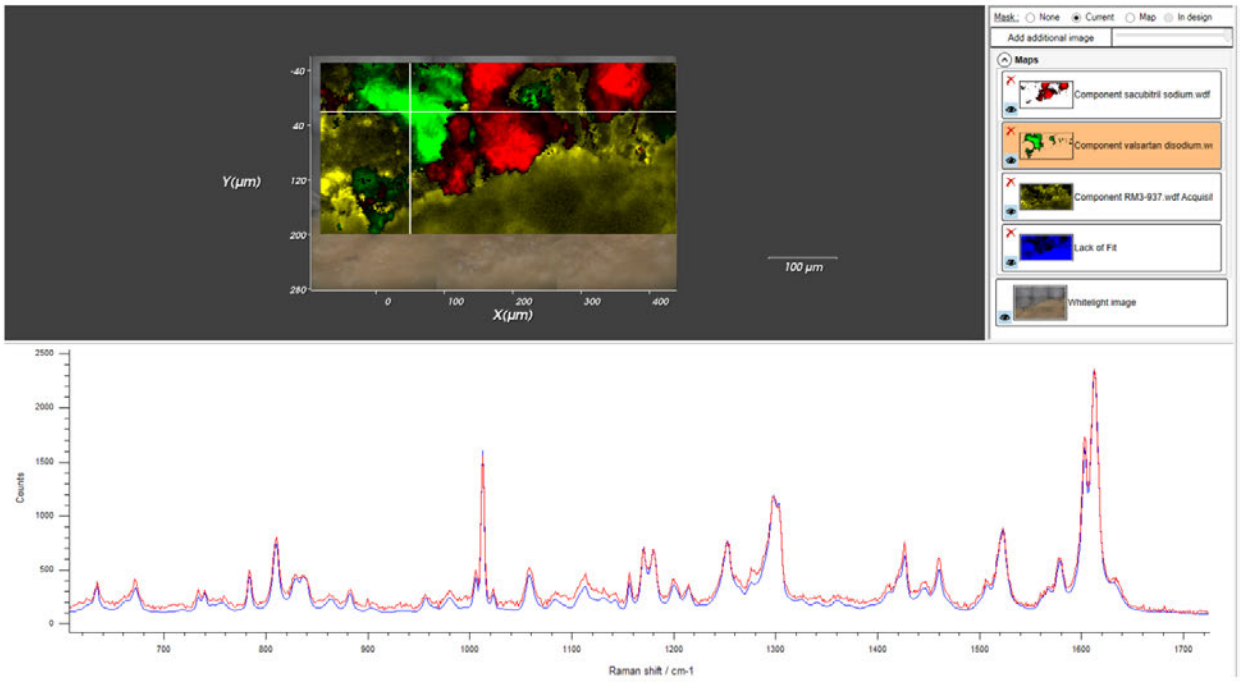
2. Even under the district court's claim construction, Novartis will likely succeed in proving infringement

The outcome will be the same under the district court's claim construction. That construction governs only the possible forms of TVS in the product, not other components. The construction requires "a solid form *of a compound* in which the amorphous form *of the compound* predominates." Add16 (emphasis added). The claimed "compound" is TVS. The court's claim construction means, then, that where there is a combination of amorphous TVS and crystalline TVS, the amorphous form must predominate over the crystalline. Add795-797(¶¶23-29). As discussed

above, there is amorphous TVS in MSN's products. And Dr. Matzger's testing reveals that the TVS is predominantly amorphous because the rest of the API in the products is not TVS but a physical mixture of separate valsartan disodium and separate sacubitril sodium. Because there is no crystalline TVS in MSN's products, the amorphous TVS necessarily "predominates" over nonexistent crystalline TVS.

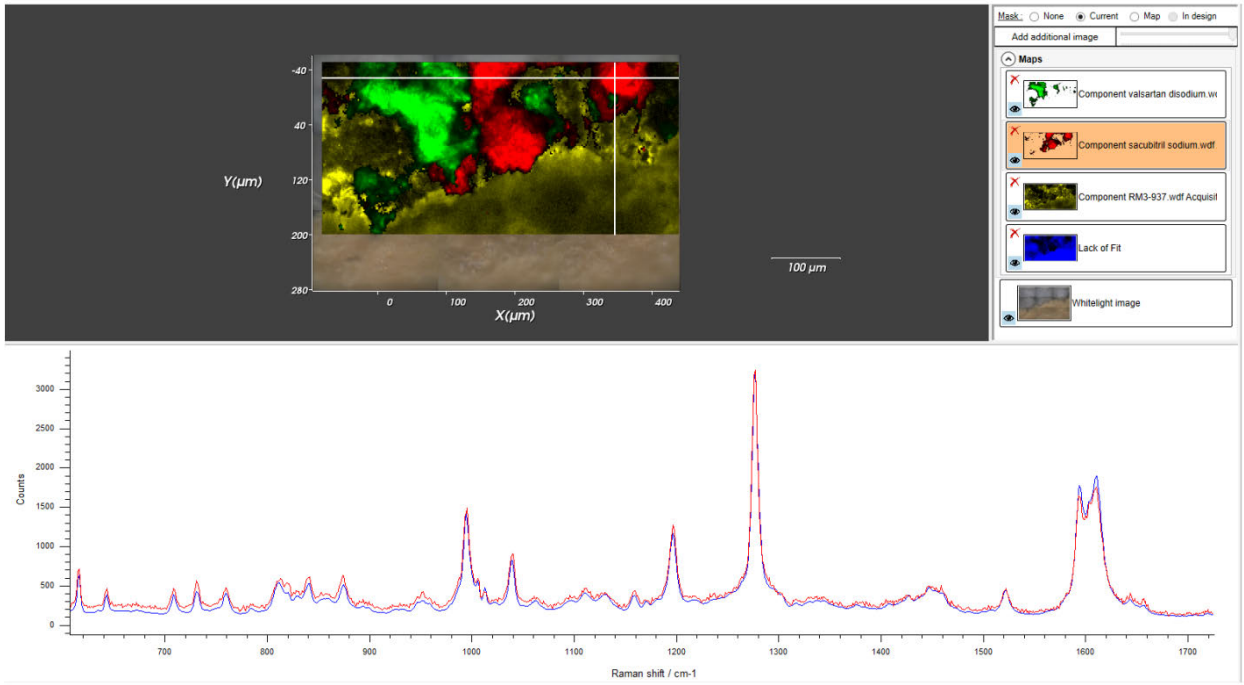
Multiple analyses by Dr. Matzger confirm that, along with small amounts of amorphous TVS, MSN's products comprise regions of separate valsartan disodium and sacubitril sodium rather than crystalline TVS. First, Raman mapping of samples of MSN's tablet, shown below, shows regions of crystalline valsartan disodium (green) and separate regions of crystalline sacubitril sodium (red). Below the maps are the Raman spectra in each region, showing a close match between the experimental spectra (red) and reference spectra (blue) that Dr. Matzger obtained for each substance. *See* Add799-801(¶¶37, 39-41).

Figure 6
Region of MSN 49/51 mg Sample Containing
Valsartan Disodium (AJM-XXVIII-2.3 Cosmic.wdf)



Add812(¶60).

Figure 7
Region of MSN 49/51 mg Sample Containing
Sacubitril Sodium (AJM-XXVIII-2.3_Cosmic.wdf)



Add812(¶60).

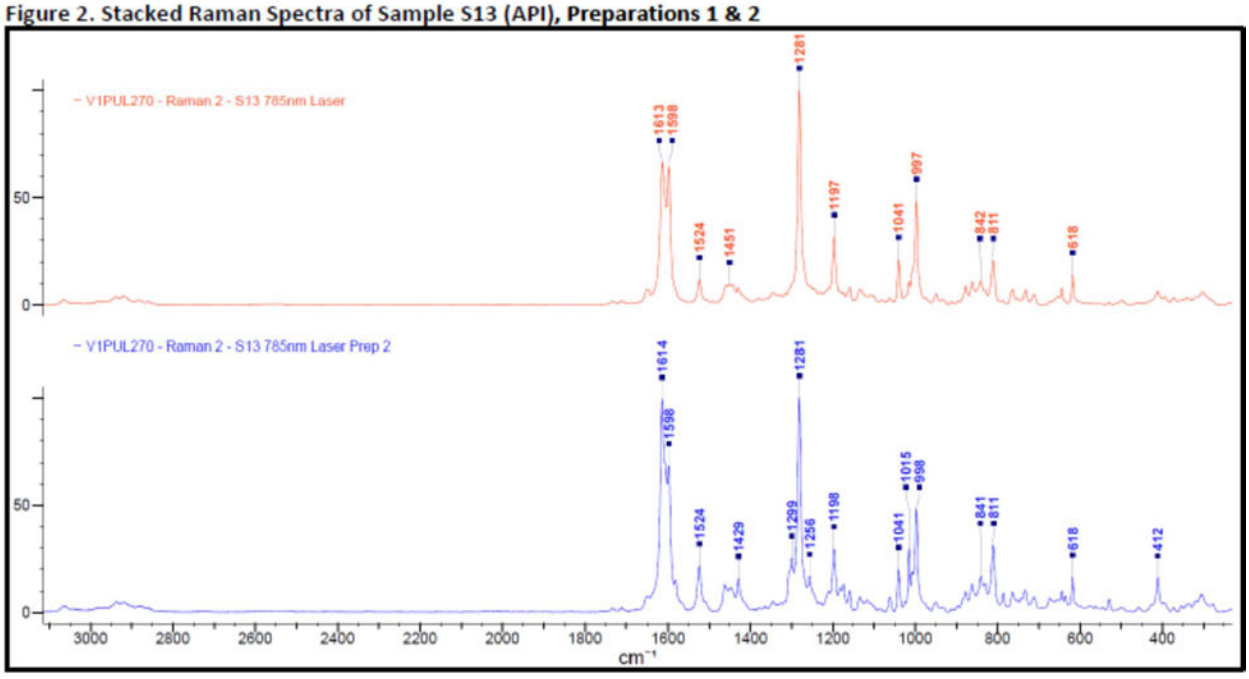
Second, Raman mapping from samples of MSN's isolated API (not yet in the final dosage form) likewise shows a heterogeneous, or physical, mixture of the two separate substances. Add801-802(¶¶42-43). The entire sample was those two substances, meaning crystalline TVS was absent. Add804(¶44).

Finally, X-ray microdiffraction on MSN's API also shows a heterogeneous physical mixture. X-ray microdiffraction is similar to the X-Ray Powder Diffraction (XRPD) on which MSN has focused, but microdiffraction is performed on small particles rather than bulk samples and so can detect heterogeneity that XRPD could not. Add805(¶46); Add827(¶86). Each microdiffraction sample produced a subset

of the features present in the bulk XRPD data, indicating the isolated API is a mixture of separate sacubitril sodium and separate valsartan disodium. Add805-807(¶¶47-49).

MSN obtained its own Raman spectra of the isolated API as part of this litigation, and the results are consistent. MSN obtained spectra from two samples. Tellingly, the spectra are different, showing heterogeneity in the API substance. As Dr. Matzger explained, the differences indicate that the API is a physical mixture of valsartan disodium and sacubitril sodium. Add832(¶¶99-100); Add1318.

Figure 2. Stacked Raman Spectra of Sample S13 (API), Preparations 1 & 2



Specifically, the first sample's Raman spectrum corresponds to crystalline sacubitril sodium alone. It matches Dr. Matzger's spectrum for that substance with, for example, a characteristic peak around 1281 cm^{-1}. Add832(¶100); *see* Add818(¶64). The additional peaks in the second sample's Raman spectrum, for example at

1299 cm^{-1}, are due to the inclusion of crystalline valsartan disodium in the sample. Add832(¶100); Add818(¶64). The district court thought that the differences between the first spectrum (orange) and the spectrum Dr. Matzger identified as a physical mixture support "what appear to be valid criticisms" of Novartis's test data. Add5-6. But the differences are explained by the first sample being sacubitril sodium alone, which is possible only in a sample from a heterogeneous physical mixture. This explanation, coupled with what the district court recognized as Novartis's valid criticisms of MSN's own data, means Novartis is likely to succeed in proving that MSN's isolated API contains no crystalline TVS (and thus amorphous TVS predominates).

These results leave no doubt about the composition of MSN's products: they contain a mixture of separate sacubitril sodium and separate valsartan disodium—along with amorphous TVS but no crystalline TVS. Thus, the amorphous form of the TVS compound necessarily predominates over the crystalline. That shows Novartis is likely to succeed in proving infringement under the district court's construction. The district court clearly erred in finding otherwise.

B. Novartis Will Suffer Irreparable Harm Absent an Injunction

MSN's threatened at-risk launch will cause Novartis immediate irreparable harm. Novartis will suffer a dramatic loss of market share, lose substantial profits, and ENTRESTO®'s price will irreversibly erode. These are classic harms that

support preserving the status quo pending appeal. Novartis is likely to show the district court clearly erred in concluding otherwise.

1. Novartis has demonstrated substantial and irreparable harm

"Evidence of head-to-head competition and lost market share can support a showing of irreparable harm." *Natera v. NeoGenomics Lab'ys*, 106 F.4th 1369, 1378 (Fed. Cir. 2024). So can evidence that "the alleged injury is not quantifiable." *Id.* This Court thus has recognized the harm, often irreparable, of forcing a patentee to compete against an infringer in a market the patentee "created with its investment in patented technology." *Douglas Dynamics v. Buyers Prods.*, 717 F.3d 1336, 1344-45 (Fed. Cir. 2013); *see Trebro Mfg. v. Firefly Equip.*, 748 F.3d 1159, 1170 (Fed. Cir. 2014).

Here, Novartis's substantial investments in ENTRESTO® created a new market, making ENTRESTO® Novartis's top-selling drug. Add913-914(¶20). That new market has generated $22 billion in cumulative worldwide sales and $3.067 billion in U.S. sales in 2023 alone. Add913-914(¶20). Novartis has consistently identified ENTRESTO® as its top "key growth driver" in recent years. Add913-914(¶20). Even Novartis's own predictions likely underestimate ENTRESTO®'s significance; Novartis has consistently under-forecasted ENTRESTO® sales. Add931-933(¶¶58-60).

An at-risk launch will crater this market and destroy Novartis's position in it. As Dr. Vellturo explains, "[g]eneric entry invariably has a profound effect on the demand for a price of the corresponding branded drug, ultimately leading to the virtual extinction of the brand." Add923-924(¶40). Those effects occur immediately, with ENTRESTO® projected to lose % of forecasted new-to-brand prescriptions in the first month after a generic launch. Add929-930(¶54).

The financial effects will be devastating. Entry of a single infringing generic product would result in lost market share, sales, and price erosion resulting in lost profits of at least number in four months. Add935(¶65). And if MSN's at-risk launch triggers the entry of additional infringing competitors, as expected, the estimated losses will be far higher. Add935(¶65).

For multiple reasons, these harms will be irreparable. First, there will be no coming back from the price erosion an at-risk launch would cause. Large third-party payers—private insurance plans, managed care organizations, Medicare, and Medicaid—account for most prescription-drug spending. Add921-922(¶¶34-35). These large payers "often refuse to agree to significant price increases and would likely resist" efforts to restore ENTRESTO®'s price following price cuts from an at-risk launch. Add937-938(¶69). This Court thus has recognized the irreparable harm from irreversible price erosion and loss of goodwill caused by an infringing generic competitor. *Abbott Lab'ys v. Sandoz*, 544 F.3d 1341, 1361-62 (Fed. Cir. 2008);

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Sanofi-Synthelabo v. Apotex, 470 F.3d 1368, 1382 (Fed. Cir. 2006). The district court's order does not address this irreversible harm. Add6-9.

Second, the total damage is unquantifiable. Even Novartis has consistently under-forecasted ENTRESTO®'s net revenues. Add931-933(¶¶58-60). That dynamic reflects increased demand driven by "recent clinical trials and updated clinical guidelines." Add933(¶61). Any lost-profits calculation would thus be difficult and likely understate Novartis's actual damages. Add931-934(¶¶58-62); *see Celsis in Vitro v. CellzDirect*, 664 F.3d 922, 930-31 (Fed. Cir. 2012) (recognizing irreparable harm based on difficult-to-quantify losses).

The district court's injunction order disagreed, but only by overlooking the factors making it likely Novartis will be undercompensated by a post-hoc damages calculation. Add6-7. Nor could "actual sales and market data" from an at-risk launch address the problem, as the district court believed. Add7 (n. 10). A generic launch would change the market fundamentally, so once MSN launches, sales and market data would not reflect the profits that ENTRESTO® would have earned in the "but-for" world without generic competition. Add940-941(¶¶73-74).

Third, it is exceedingly unlikely MSN could fully compensate Novartis's losses. Add934-937(¶¶63-67). MSN and Novartis financial information [redacted] The district court stated it was

"confident" in MSN's ability to pay, but largely because it discounted Novartis's expected damages without a reasonable basis. Add7-8. It also seems to have credited MSN's baseless and speculative assertion that it might "mitigate" its exposure by "acquir[ing] insurance coverage" or limiting distribution of its products. Add8-9. If anything, that MSN has considered these options further undercuts its unsupported representations that its current financial condition is sufficient to make Novartis whole.

Additionally, if Novartis proves infringement under 35 U.S.C. §271(e)(2) (as is likely), it will be entitled—without any showing on the equities—to a stay of MSN's ANDA approval until the '918 patent expires. 35 U.S.C. §271(e)(4)(A); *Vanda Pharms. v. West-Ward Pharms. Int'l*, 887 F.3d 1117, 1138 (Fed. Cir. 2018). MSN's at-risk launch would render that relief all-but worthless, further demonstrating Novartis cannot be made whole after the judgment.

Fourth, defendants' at-risk launch could force Novartis "to scale down" "investments," including in "the ENTRESTO sales force" and "patient support programs." Add938(¶70). Novartis would be unable to restore these investments to previous levels later. Add939(¶72). ENTRESTO®'s sales force also supports other medications, and "[t]he accelerated reduction" in "sales force personnel and resources would thus likely translate" to non-compensable lost sales for those products. Add941(¶75). Reducing programs to educate patients and physicians

about the relative superiority of valsartan-sacubitril treatments will lead to lost sales volume "unlikely ever to be recovered." Add940-941(¶74). The district court was wrong to dismiss these harms as "profit-maximizing business decisions." Add7. This Court has recognized similar facts as supporting irreparable harm. *Celsis*, 664 F.3d at 930 ("loss of business opportunities"); *Apotex*, 470 F.3d at 1383 ("potential reduction in work force").

2. MSN's infringement would cause Novartis's harm

The irreversible harm MSN's at-risk launch causes will be the result of MSN's infringement. The causal nexus analysis is "flexible." *Apple v. Samsung Elecs.*, 809 F.3d 633, 641-642 (Fed. Cir. 2015) ("*Apple IV*"). It requires only "a showing of *some* causal nexus" between the infringement and the harm. *Apple v. Samsung Elecs.*, 678 F.3d 1314, 1324 (Fed. Cir. 2012) ("*Apple I*") (emphasis added). Where (as here) the irreparable harm stems from competition with an infringing product, the patentee need only "show 'some connection' between the patented features and the demand for the infringing products" (*Apple IV*, 809 F.3d at 642), not that the infringing features are "the exclusive or predominant" cause of the harm. *Genband US v. Metaswitch Networks*, 861 F.3d 1378, 1383 (Fed. Cir. 2017) (quotation marks and emphasis omitted).

That standard is more than satisfied here. [redacted]

[redacted] MSN manufacturing information

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[redacted] MSN manufacturing information [redacted]

That easily shows "some connection" between the infringement and Novartis's harm from MSN's launch. *Apple IV*, 809 F.3d at 641. Indeed, this Court recently confirmed that a patentee demonstrates causal nexus when infringement is a prerequisite to offering the feature that drives demand. In *Natera*, the Court concluded that an unclaimed feature—"highly sensitive tumor-informed testing"—drove demand, and that the feature was "impossible to achieve without" infringement. 106 F.4th at 1380. That was sufficient to "tie[]" consumer demand (and thus the patentee's harm) to the infringement. *Id.* [redacted] MSN manufacturing information [redacted]

Nor does it matter that ENTRESTO® does not contain amorphous TVS. "In multiple instances, this [C]ourt has held that a party that does not practice the asserted patent may still receive an injunction when it sells a competing product." *Trebro*, 748 F.3d at 1171 (collecting cases, including from preliminary-injunction context). Similarly, that the '918 patent is not listed in the Orange Book for ENTRESTO® does not defeat Novartis's showing of irreparable harm. This Court

has upheld a finding of irreparable harm and a preliminary injunction barring sales of an infringing generic even though the infringed patent was not Orange Book-listed. *Glaxo Grp. v. Apotex*, 376 F.3d 1339, 1344-45 (Fed. Cir. 2004); *Glaxo Grp. v. Apotex*, 64 F. App'x 751, 756 (Fed. Cir. 2003).

II. THE EQUITIES FAVOR AN INJUNCTION

The equities and the public interest also favor an injunction. This Court has "long acknowledged the importance of the patent system in encouraging innovation." *Apotex*, 470 F.3d at 1383. That is especially true in the pharmaceutical context because the incentive to invest "in drug research and development" "would be adversely affected by taking market benefits away from the patentee and giving them to [an] accused infringer." *Celsis*, 664 F.3d at 931-32. Those interests are amplified here because, as explained, generic entry would also cause heart-failure patients to suffer from reduced investments in patient-support programs and educational campaigns. Add943-944(¶81). Such permanently reduced investment in patient outreach may cause a significant number of heart-failure patients to forgo treatment with any sacubitril/valsartan drug—whether ENTRESTO® or a generic—thereby depriving them of the significant clinical benefits the combination offers over other drugs. Add937-938(¶¶69-70). And contrary to the district court's reasoning, this harm cannot be offset by the availability of cheaper generics. Patients who never learn about sacubitril/valsartan will not take it, regardless of its price.

The significant harm to Novartis and the public outweighs any harm MSN would suffer. The district court suggested MSN would lose a "first-mover advantage," but had no basis for that unsupported speculation given that other generics are already approved and have chosen not to launch at risk. *Contra* Add9.

III. THIS COURT SHOULD IMMEDIATELY ENTER A TEMPORARY INJUNCTION PENDING THIS MOTION'S RESOLUTION

This Court should immediately enter a temporary injunction to maintain the status quo while considering this motion. Federal appellate courts, including this one, have regularly granted temporary relief to "freeze legal proceedings until the court can rule on a party's request for expedited relief." *United States v. Texas*, 144 S. Ct. 797, 798 (2024) (Barrett and Kavanaugh, J.J., concurring) (collecting cases); *Marine Polymer Techs. v. HemCon*, 395 F. App'x 701, 702 (Fed. Cir. 2010) (granting administrative stay to preserve status quo). Rather than "consideration of the merits of the stay application" the purpose is to "buy[] the court time to deliberate" on the stay. *Texas*, 144 S. Ct. at 798.

IV. THIS APPEAL SHOULD BE EXPEDITED

MSN has agreed to this briefing schedule for this appeal:

- Opening: 7 days (8/20)
- Response: 7 days (8/27)
- Reply: 3 days (8/30)
- Appendix: 3 days (9/2)
- Argument: As soon as practicable.

CONCLUSION

This Court should enjoin an at-risk launch of MSN's generic versions of ENTRESTO®, temporarily while resolving this motion and then until the appeal is resolved, and expedite this appeal.

Dated: August 13, 2024

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

The foregoing filing complies with the relevant type-volume limitation of the Federal Rules of Appellate Procedure and Federal Circuit Rules because the filing has been prepared using a proportionally spaced typeface and includes 5,132 words, excluding the parts of the brief exempted by the Rules.

Dated: August 13, 2024 /s/ Deanne E. Maynard

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